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PENTACYCLIC TRITERPENES FROM Maytenus quadrangulata (CELASTRACEAE): ISOLATION, SEMISYNTHESIS, AND CYTOTOXIC ACTIVITY

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The genus *Maytenus*, one of the largest within the Celastraceae family, is widely recognized for its pharmacological potential, exhibiting diverse biological activities such as anti-inflammatory, antiulcerogenic, antioxidant, antibacterial, and analgesic effects.[1,2] *Maytenus quadrangulata*, a Brazilian species popularly known as "espinho-de-deus", has been previously studied for its hexane leaf extract, which demonstrated significant cytotoxic effects from isolated triterpenes.[3] In this context, the present study aims, for the first time, to perform a detailed analysis of the compounds present in the chloroform extract of *M. quadrangulata* leaves. The chloroform extract was subjected to successive column chromatography (CC), leading to the isolation of the triterpene friedelane-3α,25-diol (**1**) and a mixture of hydroxylated triterpenes (**M1**). To separate the constituents of mixture **M1**, an acetylation reaction was performed, followed by CC purification. This process yielded five new semisynthetic triterpenes: friedelane-3α,29-yl diacetate (**2**), friedelane-3α,11β-yl diacetate (**3**), friedelane-3α,25-yl diacetate (**4**), 3β-hydroxyfriedelane-24-yl acetate (**5**), and 11β-hydroxyfriedelane-3α-yl acetate (**6**), along with two previously reported triterpenes: friedelane-3α-yl acetate (**7**) and 3β,24-yl diacetate (**8**). Furthermore, the triterpene friedelane-3β,24-diol (**9**) was obtained by hydrolysis of compound **5**. Compounds **1–3**, **5–7**, and **9** were evaluated for their cytotoxic activity against leukemia cell lines (K-562, THP-1) and healthy lung fibroblast cells (WI-26VA4). The IC_{50} values of the tested compounds ranged from 28.9 µM to over 300 µM for THP-1 and K-562 cells, with selectivity indices between 0.3 and 3.3. The compounds showed low to moderate cytotoxicity relative to the positive controls (etoposide and cytarabine).

Figure 1: Chemical structure of compounds **1–9**

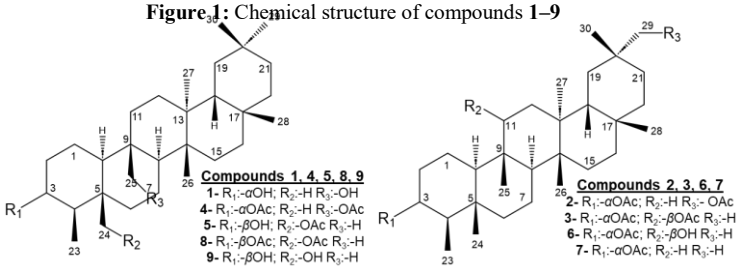

Table 1: IC_{50} values and selectivity index of the tested compounds

Compounds	THP-1	SI	K562	SI	Wi-26VA4
1	245.6 ± 12.5	0.3	45.9 ± 4.8	1.5	70.9 ± 5.6
2	210.5 ± 8.9	ND	66.5 ± 5.4	ND	> 300
3	230.4 ± 9.1	1.0	74.2 ± 6.3	3.3	244.5 ± 10.8
5	81.3 ± 8.8	1.3	58.9 ± 4.5	1.8	105.5 ± 10.3
6	120.8 ± 7.1	0.7	28.9 ± 3.6	3.1	88.9 ± 6.0
7	> 300	ND	> 300	ND	> 300
9	> 300	ND	35.4 ± 5.6	ND	> 300
Etoposide	ND	ND	34.6 ± 4.2	ND	ND
Cytarabine	40.7 ± 4.4	ND	ND	ND	ND
Doxorubicin	ND	ND	ND	ND	1.9 ± 0.9

*ND = not determined

Keywords: *Triterpenes, Celastraceae, Cytotoxic activity, Maytenus quadrangulata*

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